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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,160	05/24/2007	Helge H. Rasmussen	U 016502-0	8069

140 7590 10/16/2009

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EXAMINER	
CLARK, SARA E	
ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
10/16/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

nyuspatactions@ladas.com

Office Action Summary	Application No.	Applicant(s)	
	10/594,160	RASMUSSEN ET AL.	
	Examiner	Art Unit	
	SARA E. CLARK	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *1,2 and 15-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/23/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL REJECTION

Receipt is acknowledged of Applicants' Amendments and Remarks, filed 7/17/2009.

Claims 5 and 6 have been amended and incorporate no new matter.

No new claims have been added.

Thus, claims 3-14 now represent all claims currently pending and under consideration.

INFORMATION DISCLOSURE STATEMENT

The information disclosure statement (IDS) submitted on 7/23/2009 was filed after the mailing date of the Office Action on 2/18/2009. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

WITHDRAWN REJECTIONS

Objections

Due to the amendment of claim 5, the objection to claim 5 has been withdrawn.

Rejections under 35 USC §112

Due to the amendment of claim 6, the rejection of claims 3-7 and 9-14 under 35 USC §112, second paragraph, for indefiniteness, has been withdrawn.

Rejections under 35 USC §103

Due to the amendment of claim 6, the rejection of claim 6 under 35 USC §103(a) as obvious over **Carson** and **Wheeldon** has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of **Carson** and **Wheeldon** further in view of **Gauthier**. See below.

MAINTAINED REJECTIONS

The following rejection is maintained from the previous Office Action dated 2/18/2009, on the ground that the references cited therein continue to read on the limitations of the amended claims.

Rejections under 35 USC §112

Claim 8 stands rejected under 35 USC §112, second paragraph, for indefiniteness. Claim 8 continues to contain typographical errors which render its meaning indefinite. Specifically, "and or" is interpreted as "and/or," and "ss; 2" is interpreted as "β_2."

Rejections under 35 USC §103

Claims 3-5 and 9-12 stand rejected under 35 USC §103(a) as obvious over **Carson** and **Wheeldon**.

Claims 7 and 8 stand rejected under 35 USC §103(a) as obvious over **Carson** and **Wheeldon** further in view of **Gauthier**. Due to the amendment to claim 6, this rejection is extended to claim 6.

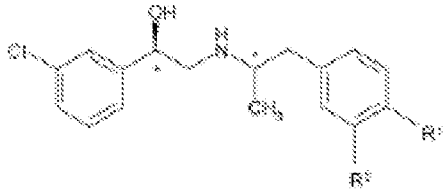
Claims 13 and 14 stand rejected under 35 USC §103(a) as obvious over **Carson** and **Wheeldon** further in view of **Cecil**.

RESPONSE TO ARGUMENTS

With regard to **Wheeldon**, Applicant contends that the reference has no bearing on the patentability of the instant claims, because BRL-35135 is not a β_3 agonist in humans (Remarks dated 7/17/2009, pp. 6-8).

However, claims 3-14 recite a method for the treatment *of an individual*, comprising the step of administering one or more β_3 adrenoceptor agonists. Since claims are given their broadest reasonable interpretation, "an individual" is interpreted to mean an individual of any species, to include dogs, rats, humans, and so forth. In addition, it was well-known that β_3 adrenoceptor expression varies widely across species, and that the cardiac effects of several β_3 adrenoceptor agonists show substantial variability across species (see, for example, Gauthier (cited in the previous Office Action, p. 427, col. 2; and Gauthier et al. (J. Pharm. Exp. Ther. 290, 687-93, 1999)). In addition, Wheeldon et al. note the possibility that a component of the chronotropic response of BRL-35135 is mediated by β_3 receptors (abstract, point 6); and more recent publications note that BRL-35135 and its *in vivo* metabolite, BRL-37344, are rodent-specific β_3 adrenoceptor agonists (see, e.g., Vicario et al., Life Sci. 62(7), 627-638, 1998, abstract and p. 628; and Arch, Rev. End. Met. Disorders 2, 385-393, 2001, figure 1, below):

Arylethanolamines



	R^1	R^2	*
BRL-37344	OCH_2CO_2H	H	RR,SS racemate
BRL-35135	OCH_2CO_2Me	H	RR,SS racemate

With regard to **Gauthier**, Applicant contends that the reference teaches away from the claimed invention because it notes that β_3 receptor antagonists "might be more desirable" in the context of heart failure (Remarks dated 7/17/2009, p. 9).

However, this statement is made at the end of the article in the context of potential therapeutic developments, which proposes hypotheses to be tested in future research:

> β-blockers specifically targeting β_1- and β_2-adrenoceptors [such as nadolol] might be more appropriate to preserve the countervailing β_3-adrenoceptor mediated pathway at earlier stages of the disease. *Conversely, when the β_3-adrenoceptor-mediated pathway might become maladaptive, nonspecific β-blockers and/or specific β3-adrenoceptor antagonists might be more desirable*.

Gauthier's point is that in later stages of heart failure, β_1- and β_2-adrenoceptors are either downregulated or desensitized, while β_3 receptors become overexpressed, at which point β_3 antagonists might be more useful. By no means is the therapeutic utility of β_3 agonists in heart failure ruled out.

The body of the reference pertains to the ability of the β_3 agonist BRL-37344 to effect the desired negative inotropic response, without interfering with the β_1/β_2-antagonist activity of nadolol, such that the combined effects of their co-administration would be especially effective in treating earlier stages of heart failure. Thus, the reference cannot reasonably said to teach away from the administration of BRL-37344 to treat individuals suffering from or susceptible to heart failure or myocardial hypertrophy, as recited by claims 6-8, but rather directly suggests the efficacy of BRL-37344 as a β_3 agonist in certain stages of heart failure.

Applicant further contends that there would have been no rationale to combine the teachings of Carson, Wheeldon, and Gauthier to arrive at the claimed invention, because the administration of β_3 agonists has yielded conflicting results (Remarks dated 7/17/2009, pp. 9-10). However, this is not persuasive because it was well-known that β_3 adrenoceptor expression varies widely across species, and thus one of ordinary skill would have been motivated to select a β_3 agonist suited to the species to be treated. Further, success had been achieved in many cases. For example, as evidenced by Gauthier (Can. J. Physiol. Pharmacol. 78, 681-90 (2000)), negative inotropic effects and decreased contractility were observed with several β_3 agonists in humans *in vivo* including BRL-37344, SR 58611A, and CL 316 243 (p. 682, col. 2). This reference reviews and reconciles divergent results with different β_3 agonists in various species, and classifies species as hyper-responders (humans and dogs), hypo-responders (rat and guinea pig) and non-responders (ferrets) (Fig. 3; p. 683). The reference also ranks four β_3 agonists effective in human heart tissue in order of decreasing potency: BRL-

37344 > SR 58611A > CL 316 243 > CGP 12177 (Table 1). Given the documented variation in β_3 agonist efficacy across species, all of which are included by the term "individuals" as recited by the instant claims, one of ordinary skill in the art would have been motivated to substitute the "rat" β_3 agonist BRL-35135 as taught by Wheeldon with the "human" β_3 agonist BRL-37344 as taught by Gauthier, with a reasonable expectation of success.

With regard to **Cecil**, Applicant contends that claims 13 and 14 relate to the addition of known treatments for stabilization of chronic disease rather than acute disease as taught by Cecil, such that the references fail to show certain features of applicant's invention. However, it is noted that the features upon which applicant relies (i.e., stabilization of chronic disease rather than acute disease) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

CONCLUSION

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARA E. CLARK whose telephone number is (571) 270-7672. The examiner can normally be reached on Mon - Thu, 7:30 am - 5:00 pm (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass, can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SARA E. CLARK/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612